Swiss canine cancer registry 1955–2008: occurrence of the most common tumour diagnoses and influence of age, breed, body size, sex and neutering status on tumour development

Grüntzig, K ; Graf, R ; Boo, G ; Guscetti, Franco ; Hässig, Michael ; Axhausen, K W ; Fabrikant, Sara I ; Welle, M ; Meier, D ; Folkers, G ; Pospischil, A

Abstract: This study is based on the Swiss Canine Cancer Registry, comprising 121,963 diagnostic records of dogs compiled between 1955 and 2008, in which 63,214 (51.83%) animals were diagnosed with tumour lesions through microscopical investigation. Adenoma/adenocarcinoma (n = 12,293, 18.09%) was the most frequent tumour diagnosis. Other common tumour diagnoses were: mast cell tumour (n = 4,415, 6.50%), lymphoma (n = 2,955, 4.35%), melanocytic tumours (n = 2,466, 3.63%), fibroma/fibrosarcoma (n = 2,309, 3.40%), haemangioma/haemangiosarcoma (n = 1,904, 2.80%), squamous cell carcinoma (n = 1,324, 1.95%) and osteoma/osteosarcoma (n = 842, 1.24%). The relative occurrence over time and the most common body locations of those tumour diagnoses are presented. Analyses of the influence of age, breed, body size, sex and neutering status on tumour development were carried out using multiple logistic regression. In certain breeds/breed categories the odds ratios (ORs) for particular tumours were outstandingly high: the boxer had higher ORs for mast cell tumour and haemangioma/haemangiosarcoma, as did the shepherd group for haemangioma/haemangiosarcoma, the schnauzer for squamous cell carcinoma and the rottweiler for osteoma/osteosarcoma. In small dogs, the risk of developing mammary tumours was three times higher than in large dogs. However, small dogs were less likely to be affected by many other tumour types (e.g. tumours of the skeletal system). Examination of the influence of sex and neutering status on tumour prevalence showed that the results depend on the examination method. In all sampling groups the risk for female dogs of developing adenoma/adenocarcinoma was higher than for male dogs. Females had a lower risk of developing haemangioma/haemangiosarcoma and squamous cell carcinoma than males. Neutered animals were at higher risk of developing specific tumours outside the genital organs than intact animals. The sample size allows detailed insight into the influences of age, breed, body size, sex and neutering status on canine tumour development. In many cases, the analysis confirms the findings of other authors. In some cases, the results are unique or contradict other studies, implying that further investigations are necessary.

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NEOPLASTIC DISEASE

Swiss Canine Cancer Registry 1955–2008: Occurrence of the Most Common Tumour Diagnoses and Influence of Age, Breed, Body Size, Sex and Neutering Status on Tumour Development

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Summary

This study is based on the Swiss Canine Cancer Registry, comprising 121,963 diagnostic records of dogs compiled between 1955 and 2008, in which 63,214 (51.83%) animals were diagnosed with tumour lesions through microscopical investigation. Adenoma/adenocarcinoma ($n = 12,293$, 18.09%) was the most frequent tumour diagnosis. Other common tumour diagnoses were: mast cell tumour ($n = 4,415$, 6.50%), lymphoma ($n = 2,955$, 4.35%), melanocytic tumours ($n = 2,466$, 3.63%), fibroma/fibrosarcoma ($n = 2,309$, 3.40%), haemangioma/haemangiosarcoma ($n = 1,904$, 2.80%), squamous cell carcinoma ($n = 1,324$, 1.95%) and osteoma/osteosarcoma ($n = 842$, 1.24%). The relative occurrence over time and the most common body locations of those tumour diagnoses are presented.

Analyses of the influence of age, breed, body size, sex and neutering status on tumour development were carried out using multiple logistic regression. In certain breeds/breed categories the odds ratios (ORs) for particular tumours were outstandingly high: the boxer had higher ORs for mast cell tumour and haemangioma/haemangiosarcoma, as did the shepherd group for haemangioma/haemangiosarcoma, the schnauzer for squamous cell carcinoma and the rottweiler for osteoma/osteosarcoma. In small dogs, the risk of developing mammary tumours was three times higher than in large dogs. However, small dogs were less likely to be affected by many other tumour types (e.g. tumours of the skeletal system).

Examination of the influence of sex and neutering status on tumour prevalence showed that the results depend on the examination method. In all sampling groups the risk for female dogs of developing adenoma/adenocarcinoma was higher than for male dogs. Females had a lower risk of developing haemangioma/haemangiosarcoma and squamous cell carcinoma than males. Neutered animals were at higher risk of developing specific tumours outside the genital organs than intact animals.

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The sample size allows detailed insight into the influences of age, breed, body size, sex and neutering status on canine tumour development. In many cases, the analysis confirms the findings of other authors. In some cases, the results are unique or contradict other studies, implying that further investigations are necessary.

Keywords: cancer registry; dog; statistical analyses; tumour

Introduction

To meet the challenge posed by the combination of potential aetiological factors in cancer, patient data and diagnoses need to be explored systematically (MacVean *et al.*, 1978; Brønden *et al.*, 2007, 2010; Vascellari *et al.*, 2009; Dobson, 2013; Waters *et al.*, 2014). This is the cornerstone of any epidemiological study of cancer that aims to investigate cancer development patterns in defined populations over time and space. The epidemiological study of cancer is therefore dependent on the availability of patient data, which are usually stored in cancer registries.

In this context, the study of companion animal cancer registries is especially valuable. Firstly, companion animals and their owners share the same environment and are therefore mostly exposed to the same environmental cancer risk factors (Bukowski and Wartenberg, 1997; Backer *et al.*, 2001; Gamlem *et al.*, 2008; Marconato *et al.*, 2009; Bettini *et al.*, 2010). Secondly, similar genetic predisposing factors for cancer development have been found for man and animals (Jónasdóttir *et al.*, 2000; Patterson, 2000; Lingaas *et al.*, 2003; Breen, 2009; Pastor *et al.*, 2009; Phillips *et al.*, 2010; Ke *et al.*, 2011). For instance, canine renal cystadenocarcinoma and nodular dermatofibrosis (Jónasdóttir *et al.*, 2000; Lingaas *et al.*, 2003) and canine osteosarcoma (Phillips *et al.*, 2010) are well-known examples of syndromes linked to genetic conditions common to both dogs and man. The former complex was linked to a specific mutation also found in people affected by a similar syndrome; in the latter a linkage to a specific locus was found in both species. These findings underline the value of comparative studies in human and veterinary oncology as part of the 'One Health' concept (Breen, 2009).

The present study is based on the Swiss Canine Cancer Registry (Grüntzig *et al.*, 2015) and highlights the influences of age, breed, body size, sex and neutering status on the development of tumours in dogs. The size of the Swiss Canine Cancer Registry, which comprises 121,963 dogs and 67,943 tumour diagnoses, allows computation of meaningful statistics. To our knowledge, the Swiss Canine Cancer Registry is the most comprehensive animal cancer registry at a national level.

Materials and Methods

Data Source

The data originated from the Swiss Canine Cancer Registry (Grüntzig *et al.*, 2015) comprising 121,963 diagnostic records of dogs provided by three veterinary diagnostic laboratories in Switzerland: the Vetsuisse Faculty Institut für Veterinärpathologie, Zürich (IVPZ), the Vetsuisse Faculty Institut für Tierpathologie, Bern (ITPA) and the Zyto/Histo Diagnostik private veterinary diagnostic laboratory (based in Rorbas Freienstein). The data sets included diagnostic records from canine samples generated by three different examination methods: post-mortem analysis (and subsequent histopathological evaluation), biopsy sampling (with subsequent histopathological examination) and cytology. Biopsy and cytology samples are hereafter called ex-vivo samples. No cases were excluded; however, some parameters were missing due to incomplete reporting by the submitting veterinarians. All diagnoses in the Swiss Canine Cancer Registry were derived from a microscopical examination.

Data Preparation

In different time periods, different terms were used for the description of age, breed, sex and neutering status. Those differences were standardized by numerical coding. The diagnoses were then coded according to the tumour topographical and morphological keys of the ICD-O-3 (Fritz *et al.*, 2013) and checked for plausibility using the original patient records. All tumour diagnoses were based on either histopathological or cytological examination. Epidermal cysts were excluded.

The data included 215 castrated male dogs with tumours in the testes. Since it is common in those cases to castrate the patient while sampling the tumour, those dogs where re-classified as entire at the moment of tumour diagnosis.

Data sets missing the information on the sex and/or status of neutering of patients were excluded from the

evaluation of the influence of these parameters on tumour development.

Breed allocation was based on information available in the diagnostic records, which was usually provided by the pet owner or by the submitting veterinarian. A declaration of one breed was accepted as reported, while a declaration comprising two breeds (in the case of an apparent mix with recognizable breeds) was categorized according to the breed mentioned first (i.e. a shepherd-cross was categorized under shepherd, a shepherd—boxer-cross likewise under shepherd and a boxer—shepherd-cross under boxer). It was assumed that the breed mentioned first was the one more obvious from the external appearance. Therefore, the breeds defined in this work cannot be considered pure breeds and a certain influence of mixed breeding must be acknowledged in the risk calculations. The proportion of manifestly non-pure breeds ranged between 0 and 18% in the breeds considered for analysis (Table 1). Because all such mixed breeds likely share at least 50% of their genetic information with the predominant breed, content of non-breed related genome is maximally 50% in these animals. This should be taken into account while interpreting the results of the statistics. As an example, for the Swiss mountain dog, the breed with the highest proportion of manifestly crossed individuals (18.4%), the unrelated genome may theoretically account for a difference of 9% in the odds ratio (OR).

A non-specific allocation such as mixed-breed, mongrel or crossbreed was categorized under crossbreed, since it was assumed that a phenotype typical for a known breed was lacking or not distinct.

The breeds/breed categories most frequently represented in the data set, each comprising at least 900 individuals, were retained for analysis of risks related to breed (Table 1). In a preliminary investigation, the breed ranking of the data set and the breed ranking of the Swiss dog population was compared in those years in which a reference population with known breed composition was available for use as a control (1963, 1999 and 2008) (Pospischil *et al.*, 2013). For those years the patient breed ranking correlated with that of the reference population, meaning that there was no significant difference in breed distribution between the Swiss dog population and the patient collective. The difference in the distribution of the individual breeds over time was controlled for year and proportional distribution.

The remaining breeds and the diagnostic records with unknown breeds were listed as 'other breeds'. The breed category Swiss mountain dog includes Appenzeller mountain dogs, Bernese mountain dogs, Entlebucher mountain dogs, large Swiss mountain dogs, Swiss mountain dogs and mountain dogs. The breed category retriever includes Chesapeake Bay retriever, curly coated retriever, flat coated retriever, golden retriever, Labrador, Nova Scotia duck tolling retriever, retriever and sandriner (golden retriever

Table 1
Frequencies of the 17 most common breeds/breed categories in the registry and their relative proportions of crossbreeds and ensuing proportion of unrelated genome

Breed/breed category	*Total number**		*Thereof obviously crossed*		*Ensuing proportion of unrelated genome*
Shepherd	12,354	(10.13%)	867	(7.02%)	3.51%
Crossbreed	12,193	(10.00%)	12,193	(100%)	NS
Retriever	11,429	(9.37%)	802	(7.02%)	3.51%
Swiss mountain dog	7,774	(6.37%)	1,410	(18.14%)	9.07%
Poodle	7,214	(5.91%)	173	(2.40%)	1.20%
Dachshund	6,499	(5.33%)	189	(2.91%)	1.46%
Boxer	6,368	(5.22%)	127	(1.99%)	0.99%
Schnauzer	2,796	(2.29%)	156	(5.58%)	2.79%
Collie	2,206	(1.81%)	223	(10.11%)	5.06%
Yorkshire terrier	2,157	(1.77%)	7	(0.32%)	0.16%
Cocker spaniel	2,127	(1.74%)	19	(0.89%)	0.45%
Setter	2,105	(1.73%)	105	(4.99%)	2.49%
Great Dane	1,598	(1.31%)	44	(2.75%)	1.38%
Dobermann	1,596	(1.31%)	72	(4.51%)	2.26%
Rottweiler	1,470	(1.21%)	63	(4.29%)	2.15%
West Highland white terrier	1,316	(1.08%)	3	(0.23%)	0.12%
Bulldog	1,016	(0.83%)	0	(0.00%)	0.00%
Parson Jack Russell terrier	981	(0.80%)	75	(7.65%)	3.83%
Other breeds (including dogs of unknown breeds)	38,764	(31.78%)	NS	NS	NS
Total of all breeds	121,963	(100%)	16,528	(13.55%)	7.78%

*Dogs were allocated to a certain breed based on the owner's claims; crossbreeds with dominant traits of a breed were included. NS, not specified.

crossed with Irish setter). The breed category setter includes English setter, Gordon setter, Irish red and white setter, Irish red setter, Irish setter and setter. The breed category shepherd includes German shepherd dog, Beauceron Berger de Beauce, white shepherd, Berger de Picardie, Berger de Savoie, Berger des Pyrénées, Groenendael, Laekenois, Malinois and Tervueren.

For the examination of the influence of body size on tumour development two groups were established. 'Large breeds' comprised the dobermann, Great Dane, retriever, rottweiler, Swiss mountain dogs, shepherd and setter. 'Small breeds' comprised the bulldog, dachshund, Parson Jack Russell, West Highland white terrier and Yorkshire terrier.

Statistical Evaluation

Data editing and statistical analyses were performed using Stata Software (Stata Corp., 2011; Stata Statistical Software: Release 12; College Station, Texas, USA). Statistical analyses were carried out using a Chi-Square/Fisher's exact test. Significant univariable variables were further integrated in a multiple logistic regression model using binary logistic models and stepwise backward procedure. The following variables were included in the model as fixed terms: sex, neutering status, breed, age, year, method of examination and canton of origin. The first four variables are random variables related to the animals and were also used for the specific evaluations on cancer frequency. The three latter variables were random factors related to time, examination method and spatial distribution. The underlying Stata model for the multiple logistic regression was <logistic vary varx1 varx2 varx3 varx4 varx5 varx6 varx7>, whereby vary = tumour, varx1 = sex, varx2 = neutering status, varx3 = breed, varx4 = age, varx5 = year of examination, varx6 = method of examination, varx7 = canton of origin. $P < 0.05$ was considered to be significant and ORs with 95% confidence intervals (CIs) were calculated. The power was set at 0.8. In the statistical evaluation, crossbreeds were used as the standard for comparisons with the remaining breeds, since they were assumed to have the largest genetic variation. For the evaluation of influence of sex and neutering status (Fig. 6) on overall tumour development, the data were divided into two subsets based on the examination method: post-mortem samples and ex-vivo samples. The results of the following three groups were compared: post-mortem samples, ex-vivo samples and all samples. For the evaluation of the influence of sex and neutering status on most common tumour diagnoses and locations (Tables 2–4), the total data set (all samples) was compared with the post-mortem sample data subset. The analyses of the influence of age on specific tumour development was biased by the low number of cases aged >15 years. Therefore, results are shown until the age of 15.

Results

The Swiss Canine Cancer Registry consists of records from 126,693 dogs that underwent pathological examination. The number of patients with confirmed tumours was 63,214 (51.83%). Some dogs were diagnosed with multiple primary tumours, adding up to a total of 67,943 diagnosed tumour lesions.

The age distribution has been previously presented (Grüntzig *et al.*, 2015). A large number of the dogs were crossbred ($n = 12{,}193$; 10.00%). Breed distribution is given in Table 1. The collective comprised 56,062 (45.97%) male dogs and 61,754 (50.63%) female dogs. The neutering status was recorded as entire in 59,902 (49.11%) dogs, neutered in 26,127 (21.42%) dogs (8,845 male, 17,731 female) and not specified in 35,934 (29.46%) dogs.

Table 2
Risk of developing the most common tumour types, comparing sexes and sampling methods

Tumour type	*Odds ratios and [95% confidence intervals] for females compared with males (OR = 1) in samples collected by*	
	All methods	Post mortem
Adenoma, adenocarcinoma	**1.337 [1.318, 1.356]**	**1.106 [1.075, 1.137]**
Fibroma, fibrosarcoma	**0.904 [0.878, 0.930]**	1.081 [0.966, 1.211]
Haemangioma, haemangiosarcoma	**0.889 [0.862, 0.917]**	**0.908 [0.842, 0.979]**
Lymphoma	**0.953 [0.929, 0.977]**	0.968 [0.926, 1.011]
Mast cell tumour	1.005 [0.984, 1.026]	0.982 [0.874, 1.103]
Melanocytic tumour	**0.843 [0.820, 0.867]**	0.969 [0.843, 1.115]
Osteoma, osteosarcoma	1.004 [0.959, 1.052]	1.031 [0.949, 1.121]
Squamous cell carcinoma	**0.888 [0.856, 0.922]**	**0.784 [0.686, 0.896]**

Statistically significant results are in bold. The number of observations was: 126,692 for all methods and 27,753 for post-mortem samples.

Table 3
Risk of developing the most common tumour types, comparing neutering status and sampling methods

Tumour type	*Neutered males compared with entire males (OR = 1)*		*Neutered females compared with entire females (OR = 1)*	
	In ex-vivo and post-mortem samples	*In post-mortem samples*	*In ex-vivo and post-mortem samples*	*In post-mortem samples*
	OR and [95%CI]	*OR and [95%CI]*	*OR and [95%CI]*	*OR and [95%CI]*
Adenoma, adenocarcinoma	**1.384 [1.218, 1.573]**	**1.730 [1.339, 2.237]**	**0.650 [0.604, 0.699]**	1.183 [0.967, 1.446]
Fibroma, fibrosarcoma	1.181 [0.984, 1.417]	0.824 [0.361, 1.880]	**1.183 [1.010, 1.386]**	1.128 [0.559, 2.276]
Haemangioma, haemangiosarcoma	0.995 [0.832, 1.188]	1.005 [0.665, 1.519]	**1.610 [1.374, 1.886]**	**2.438 [1.606, 3.703]**
Lymphoma	**1.150 [1.006, 1.315]**	**1.558 [1.130, 2.150]**	**1.349 [1.194, 1.525]**	**2.295 [1.694, 3.111]**
Mast cell tumour	**1.150 [1.008, 1.313]**	**3.461 [1.515, 7.910]**	**1.190 [1.080, 1.312]**	**2.980 [1.355, 6.551]**
Melanocytic tumour	0.962 [0.817, 1.133]	0.868 [0.251, 3.002]	**1.407 [1.216, 1.627]**	**4.425 [1.619, 12.094]**
Osteoma, osteosarcoma	**1.555 [1.218, 1.985]**	**2.022 [1.151, 3.554]**	1.210 [0.982, 1.491]	1.420 [0.887, 2.275]
Squamous cell carcinoma	0.771 [0.588, 1.010]	**3.811 [1.515, 9.585]**	**1.287 [1.051, 1.576]**	1.969 [0.502, 7.719]

Statistically significant results are in bold. The number of observations was: 43,006 for ex-vivo and post-mortem samples and 7,357 for post-mortem samples for neutered versus entire males and 46,387 for ex-vivo and post-mortem samples and 6,144 for post-mortem samples for neutered versus entire females.

The following results show the influence of breed on the most common tumour types, as well as of age, body size, sex and neutering status on the overall and specific tumour occurrence. In addition, the influence of sex and neutering status on the anatomical locations is reported. Their occurrence patterns over the years are also included. The classification and distribution of the tumour species of the data set is presented in Supplementary Table 1.

Table 4
Risk of developing a tumour in the most common locations, comparing sexes and sampling methods

Tumour location	*Females compared with males (OR = 1)*	
	In ex-vivo and post-mortem samples	*In post-mortem samples*
	OR and [95%CI]	*OR and [95%CI]*
Skin	**0.895 [0.886, 0.905]**	0.964 [0.902, 1.029]
Mammary gland	**3.264 [3.163, 3.369]**	**4.115 [3.486, 4.858]**
Soft tissues	**1.027 [1.011, 1.043]**	0.930 [0.886, 0.975]
Blood, haemopoietic system	**0.912 [0.880, 0.946]**	0.982 [0.930, 1.038]
Neoplasia of bones, joints, cartilage	0.975 [0.936, 1.016]	0.961 [0.892, 1.035]
Endocrine gland	0.996 [0.951, 1.043]	**1.089 [1.032, 1.15]**
Gastrointestinal tract	**0.741 [0.726, 0.756]**	1.005 [0.962, 1.050]
Lymph nodes	**0.923 [0.852, 0.999]**	0.942 [0.837, 1.060]
Oral cavity, pharynx	**0.954 [0.911, 0.999]**	0.964 [0.846, 1.097]
Respiratory system, intrathoracic organs	**0.948 [0.914, 0.982]**	1.024 [0.979, 1.071]
Urinary organs	1.034 [0.965, 1.108]	1.059 [0.951, 1.178]
Unspecified location	**1.032 [1.016, 1.047]**	0.968 [0.936, 1.001]

Significant results in bold. The number of observations was 126,692 for ex-vivo and post-mortem samples and 27,753 for post-mortem samples.

Adenoma/Adenocarcinoma (ICD-O 8140)

Adenomas/adenocarcinomas (n = 12,293, 18.09%) were the most common tumour diagnosed overall. From 1955 to 1985, approximately 30–40% of the diagnosed tumours were adenomas/adenocarcinomas. After 1985, the frequency of these diagnoses progressively dropped to 12% in 2008 (Fig. 1). Adenomas/adenocarcinomas were most commonly diagnosed in the mammary gland (n = 6,805; 55.36%) and in the gastrointestinal tract (n = 1,020; 8.30%). Using multiple regression analysis, the ORs of the dog breeds/breed categories developing an adenoma/adenocarcinoma were compared with those of the crossbreds (OR = 1). The Yorkshire terrier, the poodle, the cocker spaniel, the collie, the dachshund and the West Highland white terrier presented with significantly higher ORs in comparison with crossbreds and the other breeds/breed categories included in the analysis. Breeds/breed categories with lower ORs were the rottweiler, the Great Dane, the bulldog, the retriever, the dobermann, the schnauzer, the Swiss mountain dog, the setter, the boxer and the shepherd (Fig. 2).

Mast Cell Tumours (ICD-O 9740)

Among the 67,943 neoplasms, 4,415 (6.50%) were diagnosed as a mast cell tumour. Between 1955 and 2008 the relative frequency of mast cell tumours rose with considerable fluctuations from 2.1% to 8.4% of the overall tumour diagnoses (Fig. 1). Mast cell tumours (n = 4,415) were mainly diagnosed in the skin (n = 4,324; 97.94%). The boxer showed outstanding significantly higher ORs of developing a mast cell tumour in comparison with crossbreds

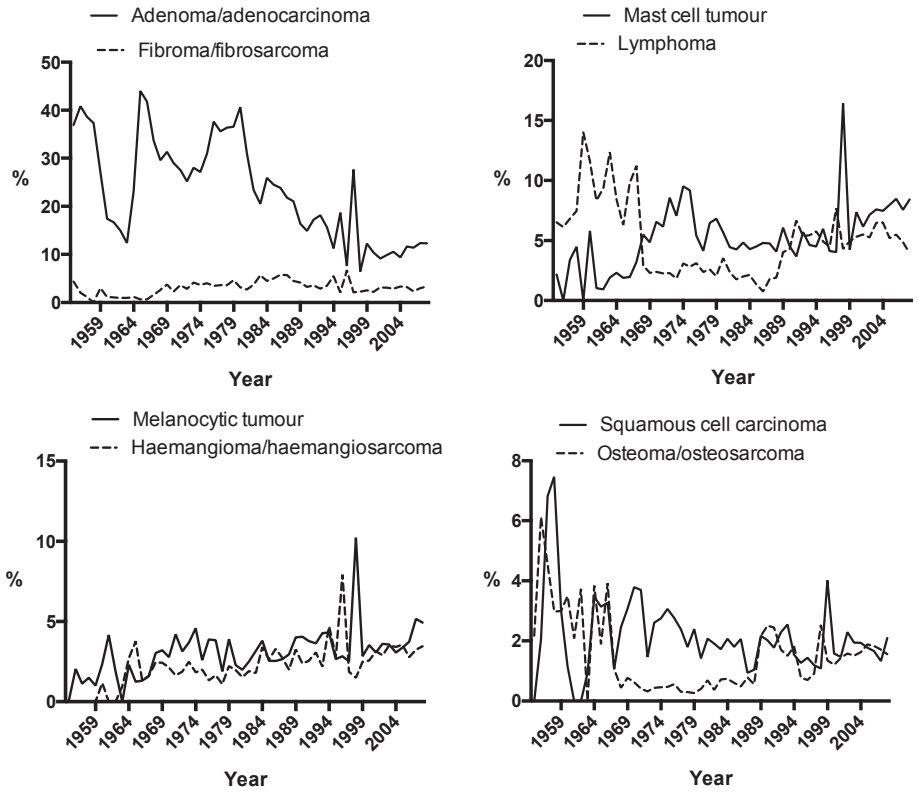

Fig. 1. Relative tumour frequencies between 1955 and 2008.

and to the other breeds/breed categories. Other breeds with higher risk were the Swiss mountain dogs, the retriever, the bulldog and the Parson Jack Russell terrier. Breeds/breed categories with lower ORs were the collie, the rottweiler, the West Highland white terrier, the shepherd, the poodle, the Yorkshire terrier, the cocker spaniel, the dobermann and the dachshund (Fig. 2).

Lymphoma (ICD-O 9590, 9591, 9700)

Among the 67,943 diagnosed tumours, 2,955 (4.35%) were lymphomas. Between 1955 and 2008 the relative frequency of lymphoma decreased from 6.52% to 3.97% per year and from 1968 to 1988 it was around 2% (Fig. 1). Lymphomas (n = 2,955) were most commonly diagnosed in the lymph nodes (n = 1,362; 46.09%) and in unspecified locations (n = 425; 14.38%), followed by the blood and haemopoietic system (n = 380; 12.86%), skin (n = 234; 7.92%), the spleen (n = 206; 6.97%) and the liver (n = 69; 2.34%). Logistic regression revealed that the rottweiler has a markedly higher OR of developing a lymphoma than crossbreds and other breeds/breed categories included in the analysis. Another breed category with higher ORs was the Swiss mountain dog. The poodle, the Yorkshire terrier, the dachshund, the retriever and the shepherd had lower ORs for lymphoma (Fig. 2).

Melanocytic Tumours (ICD-O 8720, 8730)

Among the 67,943 neoplasms diagnosed, 2,466 (3.63%) were melanocytic tumours. From 1955 to 2008 the relative frequency of melanocytic tumours rose from under 2% to over 4% (Fig. 1). The most common anatomical locations for melanocytic tumours (n = 2,466) were the skin (n = 2,309; 93.6%) and the oral cavity/nasopharynx (n = 106; 4.3%). Multiple regression analysis revealed that the ORs for the following dog breeds/breed categories of developing a melanocytic tumour were higher than those of crossbreds and the other breeds/breed categories included in the analysis: the setter, the schnauzer, the rottweiler, the retriever, the poodle, the dobermann, the dachshund and the cocker spaniel. The bulldog, the West Highland white terrier, the collie, the boxer and the Great Dane presented with lower ORs for melanocytic tumours (Fig. 2).

Fibroma/Fibrosarcoma (ICD-O 8810, 8812)

Among the 67,943 tumours, 2,309 (3.40%) were diagnosed as a fibroma/fibrosarcoma. Between 1960 and 1996 the relative frequency of fibroma/

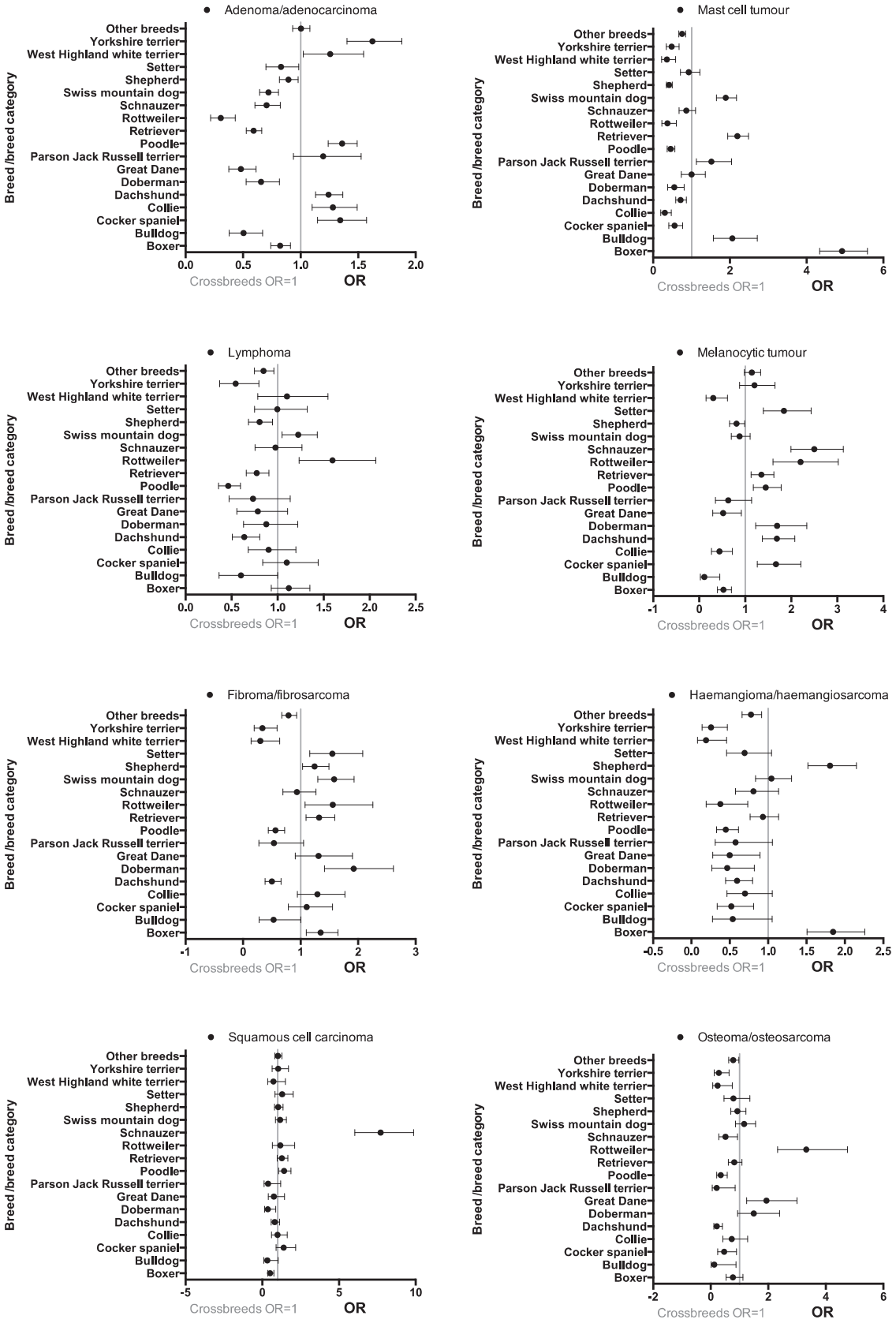

Fig. 2. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common dog breeds/breed categories of developing specific tumours compared with those for crossbreds (OR = 1). The number of observations was 126,692.

fibrosarcoma increased with several fluctuations from 1.16% to 6.71% of the total tumour number. From 1996 to 2008 their relative frequency was between 2.10% and 3.56% (Fig. 1). The most common anatomical locations for fibroma/fibrosarcoma (n = 2,309) were the soft tissues (n = 1,080; 46.77%) and the skin (n = 1,040; 45.04%). The setter, the Swiss mountain dog, the rottweiler, the retriever, the dobermann, the boxer and the shepherd had higher ORs of developing fibroma/fibrosarcoma than did crossbreds and the other breeds/breed categories included in the analysis. The West Highland white terrier, the Yorkshire terrier, the dachshund and the poodle presented with lower ORs for fibroma/fibrosarcoma (Fig. 2).

Haemangioma/Haemangiosarcoma (ICD-O 9120, 9121)

Among the 67,943 diagnosed tumours, 1,904 (2.80%) were a haemangioma/haemangiosarcoma. Between 1955 and 2008 the relative frequency of these tumours rose from 0 to 3.45%, reaching a peak of 7.92% in 1996 (Fig. 1). The most common anatomical locations for haemangioma/haemangiosarcoma (n = 1,904) were soft tissues (n = 1,203, 63.18%) and the skin (n = 459; 24.11%), followed by the blood/haemopoietic system (n = 113; 5.93%). The shepherd (OR 1.806 [CI = 1.518, 2.150]) and the boxer (OR 1.850 [CI = 1.506, 2.261]) showed higher ORs of developing a haemangioma/haemangiosarcoma than crossbreds and the other breeds/breed categories included in the analysis. The West Highland white terrier, the Yorkshire terrier, the rottweiler, the poodle, the dobermann, the Great Dane, the cocker spaniel and the dachshund presented with lower ORs for haemangioma/haemangiosarcoma (Fig. 2).

Squamous Cell Carcinoma (ICD-O 8070, 8071, 8078)

Among the 67,943 tumours, 1,324 (1.95%) were diagnosed as a squamous cell carcinoma. After a peak of 7.46% in 1958 the relative frequency of squamous cell carcinoma fluctuated between 0.94% and 4.02% of the overall tumour diagnoses until 1999. From 2000 to 2008 it was between 1.47% and 2.29% (Fig. 1). The high numbers in the 1950s might result from a bias due to the low amount of tumour data available from this period. The most common anatomical locations for squamous cell carcinoma (n = 1,324) were unspecified locations (n = 615; 46.5%), the skin (n = 601; 45.4%) and the oral cavity/nasopharynx (n = 56; 4.23%). Here, results for the schnauzer revealed a seven-fold higher risk (OR 7.712 [CI = 6.031, 9.860]) of developing a squamous cell carcinoma than the other breeds/breed categories included in the analysis. The boxer presented with a lower OR for squamous cell carcinoma (Fig. 2).

Osteoma/Osteosarcoma (ICD-O 9180)

Among the 67,943 tumours, 842 (1.24%) were diagnosed as an osteoma/osteosarcoma. From 1955 to the late 1960s the relative frequency of osteoma/osteosarcoma was variable, ranging between 6% and 0% of the overall tumour diagnoses. In the 1970s and 1980s it was constantly under 1%. Up to 2008 it rose to 1.56%, with two peaks over 2% in the 1990s (Fig. 1). The most common anatomical locations for osteoma/osteosarcoma were bones and joints (n = 746; 88.60%), followed by skin (n = 26; 3.08%). The rottweiler (OR 3.321 [CI = 2.321, 4.752]) and the Great Dane (OR 1.936 [CI = 1.248, 3.003]) presented with a higher risk of developing an osteoma/osteosarcoma than crossbreds and the other breeds/breed categories included in the analysis. The bulldog, the dachshund, the West Highland white terrier, the Parson Jack Russell terrier, the Yorkshire terrier, the poodle, the cocker spaniel and the schnauzer presented with lower ORs for osteoma/osteosarcoma (Fig. 2).

Influence of Age on Overall Tumour Development

Analyses of the influence of age revealed that the risk of developing adenoma/adenocarcinoma, melanocytic tumours and squamous cell carcinoma increased almost constantly with age. The risk of developing mast cell tumours, fibroma/fibrosarcoma, haemangioma/haemangiosarcoma and osteoma/osteosarcoma was only moderately influenced by increasing

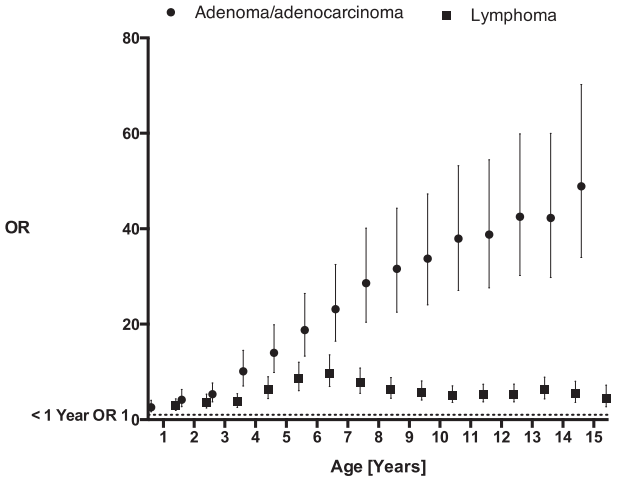

Fig. 3. Odds ratios (ORs) and 95% confidence intervals (CIs) for patients at different ages of developing different tumour types compared with patients aged <1 year (OR = 1). The number of observations was: 126,692 for adenoma/adenocarcinoma and 126,665 for lymphoma.

age after the age of 3, 4, 5 and 6 years, respectively. The risk of developing a lymphoma increased constantly with age until 6 years and decreased thereafter (Figs. 3 and 4).

Influence of Breed on Overall Tumour Development

Boxer (OR 1.700 [CI = 1.592, 1.815]), cocker spaniel (OR 1.504 [CI = 1.365, 1.658]), poodle (OR 1.443 [CI = 1.354, 1.537]), Swiss mountain dog (OR 1.357 [CI = 1.278, 1.440]), dachshund (OR 1.305 [CI = 1.223, 1.392]), setter (OR 1.299 [CI = 1.179, 1.431]), schnauzer (OR 1.289 [CI = 1.182, 1.405]) and retriever (OR 1.278 [CI = 1.211, 1.348]) were at higher risk of developing a tumour than were crossbreds. Great Dane (OR 0.532 [CI = 0.475, 0.596]), bulldog (OR 0.615 [CI = 0.537, 0.704]), West Highland white terrier (OR 0.701 [CI = 0.622, 0.789]), Parson Jack Russell terrier (OR 0.791 [CI = 0.690, 0.906]), rottweiler (OR 0.829 [CI = 0.739, 0.929]), dobermann (OR 0.833 [CI = 0.747, 0.929]), collie (OR 0.840 [CI = 0.764, 0.923]), shepherd (OR 0.872 [CI = 0.827, 0.919]) and Yorkshire terrier (OR 0.897 [CI = 0.816, 0.986]) were at lower risk of developing a tumour than crossbreds (Fig. 5). There was no generally higher risk for defined breeds/breed categories as a whole group compared with mixed breeds.

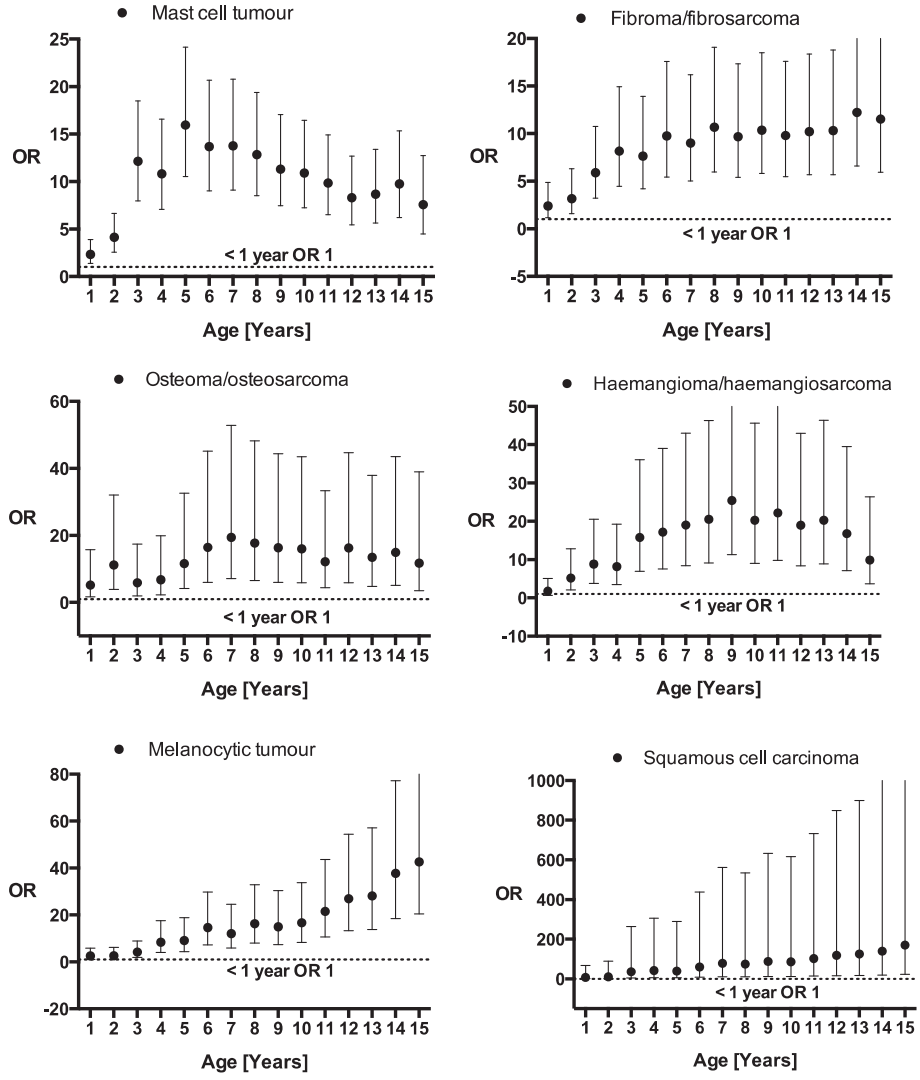

Fig. 4. Odds ratios (ORs) and 95% confidence intervals (CIs) for patients at different ages of developing different tumour types compared with patients aged <1 year (OR = 1). The number of observations was: 126,682 for mast cell tumour, 126,665 for fibroma/fibrosarcoma, 126,411 for osteoma/osteosarcoma; 126,593 for haemangioma/haemangiosarcoma; 126,651 for melanocytic tumours and 126,665 for squamous cell carcinoma.

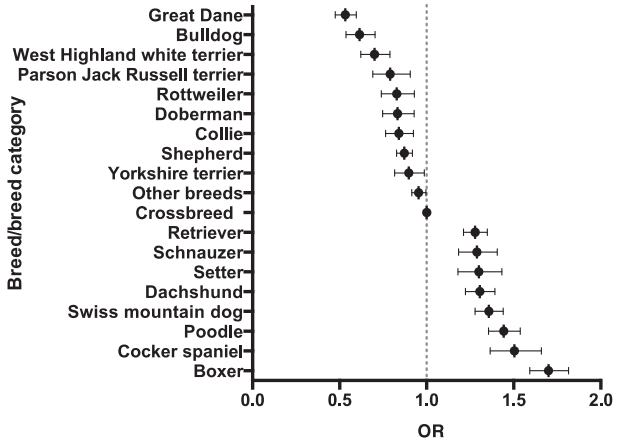

Fig. 5. Odds ratio (OR) for defined breeds/breed categories of developing a tumour compared with crossbreds. The number of observations was 126,692.

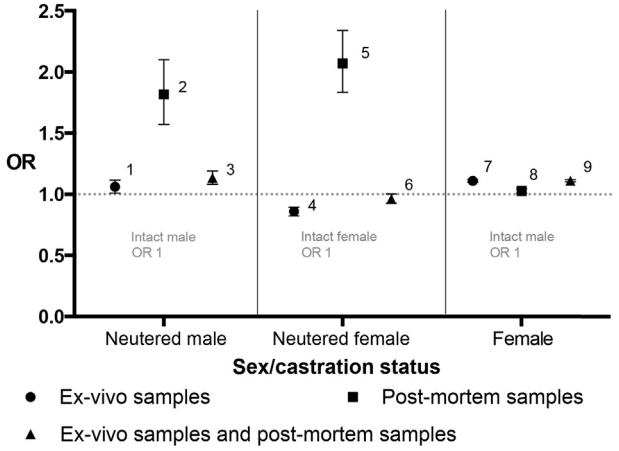

Fig. 6. Odds ratios (OR) of developing a tumour by sex and castration status, subclassified by examination method. The number of observations was: [1] 35,649; [2] 7,357; [3] 43,006; [4] 40,243; [5] 6,144; [6] 46,387; [7] 95,746; [8] 26,733; [9] 122,479.

Influence of Body Size on Overall Tumour Development

There was no general difference in the risk of developing a tumour for either body size group. However, the small breed group was three times more frequently affected by tumours of the mammary glands (OR 3.034 [CI = 2.834, 3.256]) and had a 54.82% higher risk of developing a tumour of the endocrine glands (OR 1.548 [CI = 1.190, 2.014]) than the large breed group. Small breeds were at less risk of developing tumours in the following locations: soft tissues (OR 0.402 [CI = 0.361, 0.448]), skin (OR 0.819 [CI = 0.774, 0.868]), retroperitoneum and peritoneum (OR 0.308 [CI = 0.141, 0.672]), respiratory system and intrathoracic organs (OR 0.430 [CI = 0.264, 0.439]), other female sexual organs (OR 0.274 [CI = 0.184, 0.408]), bones, joints and articular cartilage (OR 0.192 [CI = 0.131, 0.282]).

Influence of Sex and Neutering Status on Overall Tumour Development

A closer look at the influence of sex and neutering status on overall tumour prevalence showed that the results depend on the examination method (Fig. 6). In post-mortem samples, tumour risk was 81.64% higher (OR 1.816 [CI = 1.570, 2.101]) for neutered males than for entire males (by definition OR = 1.000). Tumour risk was two times higher (OR 2.070 [CI = 1.831, 2.340]) for neutered females than for entire females. In ex-vivo samples, tumour risk was only 6.18% higher (OR 1.062 [CI = 1.010, 1.117]) for neutered males than for entire males. Tumour risk was 14.20% lower (OR 0.858 [CI = 0.823, 0.894]) for neutered females than for entire females (Fig. 6).

Influence of Sex and Neutering Status on Specific Tumour Development

Hereafter, only results significant in both investigated groups (i.e. the total data set and the subset of post-mortem samples) are reported. All results are presented in Tables 2–5. The distribution of tumour locations for the investigated groups is presented in Supplementary Tables 2–5.

The ORs for female dogs of developing an adenoma/adenocarcinoma were significantly higher than those for male dogs. Females presented with lower ORs for haemangioma/haemangiosarcoma and squamous cell carcinoma than males (Table 2).

Neutered male dogs presented with higher ORs of developing the following tumours than entire male dogs: adenoma/adenocarcinoma, lymphoma, mast cell tumour and osteoma/osteosarcoma (Table 3).

Neutered female dogs had lower ORs of developing adenoma/adenocarcinoma than entire females. Neutered female dogs presented with higher ORs for the following tumours: haemangioma/haemangiosarcoma, lymphoma, mast cell tumour and melanocytic tumour (Table 3).

Influence of Sex and Neutering Status on Tumour Location

Female dogs presented with higher ORs of developing mammary gland tumours than male dogs (Table 4).

Neutered male dogs presented with higher ORs for skin tumours, tumours of the blood and the haemopoietic system, tumours of the endocrine glands, the respiratory system and intrathoracic organs and unspecified locations than entire male dogs (Table 5).

Neutered female dogs presented with higher ORs for skin and soft tissue tumours, tumours of the blood

Table 5
Risk of developing a tumour in the most common locations, comparing neutering status and sampling methods

Tumour location	*Neutered males versus entire males (OR = 1)*		*Neutered females versus entire females (OR = 1)*	
	In ex-vivo and post-mortem samples	*In post-mortem samples*	*In ex-vivo and post-mortem samples*	*In post-mortem samples*
	OR and [95%CI]	*OR and [95%CI]*	*OR and [95%CI]*	*OR and [95%CI]*
Skin	**1.088 [1.020, 1.161]**	**2.303 [1.473, 3.601]**	**1.208 [1.146, 1.274]**	**2.226 [1.637, 3.028]**
Mammary gland	1.099 [0.842, 1.434]	0.639 [0.077, 5.317]	**0.411 [0.383, 0.440]**	**0.574 [0.408, 0.806]**
Soft tissues	**1.352 [1.247, 1.466]**	1.169 [0.843, 1.621]	**1.278 [1.196, 1.366]**	**2.226 [1.637, 3.028]**
Blood, haemopoietic system	**1.385 [1.069, 1.795]**	**1.974 [1.248, 3.123]**	**1.549 [1.208, 1.986]**	**1.970 [1.251, 3.102]**
Bones, joints, cartilage	**1.492 [1.203, 1.850]**	1.475 [0.881, 2.470]	**1.258 [1.043, 1.517]**	1.136 [0.714, 1.807]
Endocrine gland	**1.563 [1.159, 2.106]**	**1.705 [1.155, 2.516]**	1.262 [0.965, 1.650]	1.101 [0.790, 1.535]
Gastrointestinal tract	1.124 [0.999, 1.265]	**1.579 [1.178, 2.118]**	**1.472 [1.296, 1.672]**	**1.975 [1.524, 2.558]**
Lymph nodes	1.551 [1.000, 2.408]	**2.318 [1.035, 5.195]**	1.105 [0.719, 1.700]	1.137 [0.465, 2.778]
Other male sexual organs (penis, prostate gland, scrotum)	1.279 [0.875, 1.870]	1.729 [0.990,3.020]	no observations	no observations
Other female sexual organs (vagina, uterus, ovary)	no observations	no observations	1.012 [0.747, 1.370]	**0.332 [0.127, 0.870]**
Oral cavity, pharynx	1.267 [0.998, 1.608]	0.358 [0.085, 1.517]	**1.348 [1.094, 1.661]**	**4.733 [2.009, 11.152]**
Respiratory system, intrathoracic organs	**1.498 [1.176, 1.909]**	**1.738 [1.306, 2.313]**	**1.554 [1.271, 1.900]**	**1.784 [1.402, 2.271]**
Urinary organs	1.419 [0.894, 2.251]	1.837 [0.947, 3.566]	**1.695 [1.203, 2.388]**	**2.656 [1.565, 4.508]**
Unspecified location	**1.133 [1.042, 1.233]**	**1.649 [1.275, 2.132]**	1.005 [0.939, 1.075]	**1.803 [1.441, 2.254]**

Significant results are in bold. The number of observations was: 43,006 for ex-vivo and post-mortem samples and 7,357 for post-mortem samples for neutered versus entire males and 46,387 for ex-vivo and post-mortem samples and 6,144 for post-mortem samples for neutered versus entire females.

and the haemopoietic system, the gastrointestinal tract, the oral cavity and pharynx, the respiratory system and intrathoracic organs and the urinary organs than entire female dogs. They had lower ORs for tumours of the mammary gland (Table 5).

To verify the results above, the investigations for neutered females versus entire females were repeated, excluding tumours of the mammary gland. The deviations from the results that included mammary gland tumours were negligible (Supplementary Tables 6–7). An exception was the result for adenoma/adenocarcinoma in post-mortem samples: neutered females had a higher risk for adenoma/adenocarcinoma than entire females when mammary tumours were excluded.

Discussion

The exceptionally large data set of the Swiss Canine Cancer Registry allowed multiple logistic regression, which was not always possible in the case of other registries and renders comparisons difficult. However, the data sets may be biased over time and further confounders could substantially influence the results. To overcome such influences specifically and to raise sensitivity, more general diagnostic terms were used. Further obstacles to comparison are typical issues related to the reproducibility of diagnoses in pathology, due to criteria for certain diagnoses changing over time and to the clearly subjective factor in histopathological diagnoses (Brønden *et al.*, 2007; Pospischil and Folkers, 2015). In this study, the influence of different time periods on techniques and state of the art in tumour diagnoses was taken into account by including the year of diagnosis as a variable in the statistical evaluation.

For the sake of simplicity only findings determined to be significant in the present work will be discussed below, while discussion of previously described results not confirmed by the present analysis will be omitted.

Adenoma/adenocarcinoma was the most frequent tumour diagnosis in dogs. Its relative proportion in total tumour diagnoses dropped from 40.6% in 1980 to 12.3% in 2008. In 1980, 92.80% of all examined canine patients ($n = 2{,}194$) were entire. However, the relative proportion of entire animals decreased to 55.6% of total patients ($n = 7{,}879$) in 2008. Since over 60% of the adenomas/adenocarcinomas were found in the sexual organs, the increasing tendency to neuter dogs could be one reason for the decrease in relative frequency of adenoma/adenocarcinoma. A similar tendency was observed for canine mammary cancers in Italy by Merlo *et al.* (2008). Another aspect is the refinement in diagnostics over time, leading to a broader diversity of tumour diagnoses.

The relative frequency of mast cell tumours, melanocytic tumours and haemangioma/haemangiosarcoma rose fairly constantly from 1955 to 2008. Since neutered female dogs are more frequently affected by these tumour types, the increase in neutering frequency over time might be partly responsible for this development.

Vascellari *et al.* (2009) reported a frequency of 3% for canine lymphomas in the animal tumour registry of two provinces in Northern Italy between 2005 and 2008, which is comparable with our data (4.88% lymphomas).

The relative frequency of fibroma/fibrosarcoma increased from 6.52% in 1955 to 10.76% in 1996 and decreased to 5.41% in 2008. These results are in contrast with the increase in feline fibroma/fibrosarcoma (20%) observed in Switzerland in the 1990s (Graf *et al.*, 2016). However, in cats a strong connection between vaccination and the development of sarcomas at sites of injection is under discussion (Henry, 2013). Such a connection has not been observed consistently in dogs.

The peaks in the relative frequency of tumour types between 1996 and 1999 were due to very high numbers of the respective tumours in the data sent in by the Vetsuisse Faculty Institut für Tierpathologie, Bern (ITPA). It is likely that these sudden increases were artificially generated by tumour studies in the institute. This is an example of factors that can skew tumour frequencies in the present study setting.

It is a well-known fact that overall tumour risk increases with age. In our data this was confirmed for adenoma/adenocarcinoma, melanocytic tumours and squamous cell carcinoma. Interestingly, the following tumour types in our study showed a frequency pattern deviating from that described above. The lymphoma risk peaked at 6 years of age. This finding is comparable with results of an Italian study (Merlo *et al.*, 2008), but contradicts data from another study from Italy, which did not, however, perform multivariate statistics (Vascellari *et al.*, 2009). There was no clear age-related incidence of haemangioma/haemangiosarcoma and mast cell tumour in patients >5 years of age. This could indicate the influence of the genetic background or other external factors.

Findings related to the effect of neutering status on tumour development were partly dependent on the examination method, specifically on whether the animal was dead or alive at the time of diagnosis. Overall tumour incidence in post-mortem samples was higher in neutered than in entire dogs, suggesting bias through investigation of mammary glands and testes in ex-vivo materials. The difference of the ORs for specific tumours in female dogs compared with male dogs was small in both sampling groups. Females were at a lower risk for haemangioma/haemangiosarcoma and squamous cell carcinoma compared with males, while they had a 33.7% higher risk for adenoma/adenocarcinoma overall. In post-mortem samples the risk was only 10.6% higher for females than for males. However, when the neutering status was taken into consideration, the difference between the sampling groups was higher, confirming the suggested bias mentioned above.

Neutered dogs were shown to have a higher risk of developing tumours in various locations other than the sexual organs, which is consistent with data from other studies (Brønden *et al.*, 2010; Torres de la Riva *et al.*, 2013; Zink *et al.*, 2014). Other authors report that tumour risk in the mammary glands in entire dogs is higher than in neutered animals, a finding supported by our data (MacVean *et al.*, 1978; Porrello *et al.*, 2006; Brønden *et al.*, 2010; Henry, 2013).

Neutered male and female dogs showed higher ORs for lymphoma and mast cell tumour. Neutered female dogs additionally showed higher ORs for melanocytic tumours and haemangioma/haemangiosarcomas, as did neutered male dogs for adenoma/adenocarcinoma and osteoma/osteosarcoma. These correlations need to be validated by future research.

In the present study, breed predispositions for neoplasia in general, arranged in descending order, were recorded in boxers, cocker spaniels, poodles, Swiss mountain dogs, dachshunds, setters, schnauzers and retrievers. In contrast, Great Danes, bulldogs, West Highland white terriers, Parson Jack Russell terriers, rottweilers, dobermanns, collies, shepherds and Yorkshire terriers showed a lower risk of developing a tumour compared with crossbreds.

Other authors report the boxer, the flat coated retriever and the golden retriever (subsets of the category of retriever in our study), the Bernese mountain dog and the Saint Bernard (subsets of the Swiss mountain dog) and the giant schnauzer (a subset of schnauzer) as being more susceptible to tumour development (Brønden *et al.*, 2010; Bell *et al.*, 2012; Dobson, 2013). German shepherd dogs were at a lower risk of tumour development in the Danish Veterinary Cancer Registry (Brønden *et al.*, 2010). These findings are roughly confirmed by our study, taking into account the differences in breed allocation.

For a better overview and clinical relevance we hereafter only discuss outstanding results of the influence of breed on the development of some specific tumours.

The boxer had an almost five times higher risk (OR 4.926 [CI = 4.343, 5.587]) of developing a mast cell tumour and a 1.85 times higher risk of

haemangioma/haemangiosarcoma (OR 1.850 [CI = 1.506, 2.261]). Similar findings have been described in the literature (Misdorp, 2004; Gough and Thomas, 2010).

Schnauzers were two times more susceptible for melanocytic tumour and seven times more susceptible for squamous cell carcinoma than crossbreds. Melanocytic tumour is known to occur more frequently in dogs with darkly pigmented skin or oral mucosa (e.g. schnauzers) (Gough and Thomas, 2010; Dobson, 2013). The OR for squamous cell carcinoma in the schnauzer was higher than expected, which might indicate either a genetic or an environmental factor associated with the geographical area from which the samples originate. Gough and Thomas (2010) report a predisposition of the schnauzer for squamous cell carcinoma of the digit in a case series.

The shepherd had higher ORs (OR 1.806 [CI = 1.518, 2.150]) of developing a haemangioma/haemangiosarcoma, which is consistent with previous reports (Gough and Thomas, 2010).

The rottweiler (OR 3.321 [CI = 2.321, 4.752]) and the Great Dane (OR 1.936 [CI = 1.248, 3.003]) had a higher risk of developing an osteoma/osteosarcoma. This tendency has also been reported in the literature (Gough and Thomas, 2010). Reported risk factors for canine osteosarcoma are high weight, high height, early neutering and breed predisposition (e.g. Irish wolfhound, Saint Bernard, Great Dane, rottweiler, Irish setter, dobermann, golden retriever, Labrador retriever and Leonberger) (Porrello *et al.*, 2006; Butler *et al.*, 2013). Genetic factors have been observed to differentiate rottweilers and golden retrievers with regard to the incidence of spontaneous appendicular osteosarcoma, independent of sex, age and histological classification (Thomas *et al.*, 2009). The most significant difference was the deletion of the *WT1* gene in 48% of the rottweiler tumour cases, while this did not occur in any of the golden retrievers. A recent study suggests that 'weight-bearing stress during the period of high proliferative activity in the long bones associated with growth may increase the risk of canine primary bone cancer' (Anfinsen *et al.*, 2015).

There was, in the present study, no significant difference between mixed breeds and the examined breeds/breed categories with regard to general cancer risk, which contrasts with the report of Brønden *et al.* (2007), who showed a twofold increased risk of developing tumours for pure breeds compared with mixed breeds. Vascellari *et al.* (2009), in addition, described the estimated crude annual incidence rate for malignant tumours as twofold higher in purebred dogs than in crossbreed dogs (Vascellari *et al.*, 2009). Different data collecting or breed definition standards might be the reason for these contradictory results. Since the declaration of breed is usually provided by the owner of the dog, it is necessary to avoid future uncertainties related to breed declaration through genetic testing. Today, the examination of the genome of dogs and the identification of single nucleotide polymorphism (SNP) haplotypes allows the classification of dog breeds on the basis of genetic relationship (Vonholdt *et al.*, 2010). This will be addressed in a follow-up study. Additionally, the breed-related risks found in the present study were confirmed through analysis of the newest data from the Swiss Canine Cancer Registry of 2009–2013 (data not shown).

Small breeds were at a higher risk of developing tumours of the mammary gland and the endocrine glands than large breeds. The following tumour locations were less likely in small breeds than in large breeds: the respiratory system and intrathoracic organs, the blood and haemopoietic system, soft tissues, skin, retroperitoneum and peritoneum, other female sexual organs, bones, joints and articular cartilage. Contrasting findings, such as a lower malignant mammary tumour incidence in small breed dogs, are suggested by Itoh *et al.* (2005). Further investigations will be necessary to verify those results. The unexpectedly high risk of developing tumours of the mammary glands for small breeds in our data could be explained by their tendency to have shorter sexual cycles (Arnold-Gloor *et al.*, 2011) and therefore increased exposure to sex hormones during oestrus.

The breeds/breed categories with lower risk of developing osteoma/osteosarcoma were breeds of small body size, with the exception of poodles and schnauzers, which show varying body sizes. These results suggest that size and castration are predisposing factors for skeletal tumours.

The large sample size in the present study allowed a detailed insight into the occurrence of the most common tumour diagnoses over time and into the influences of age, breed, body size, sex and neutering status on canine tumour development. Through the inclusion of influencing variables in the statistics, bias factors such as the examination method or the year of diagnosis were controlled. Naturally, not all environmental tumour risk factors were recorded in this retrospective cancer registry and therefore could not be included in the statistical evaluation. The clinical relevance still has to be elucidated.

In many cases, the results of the analysis of the Swiss Canine Cancer Registry confirm the findings of other authors. In some cases, the results were unique or contradicted other studies, implying that further investigations are necessary.

The reproducibility of cancer epidemiological studies is greatly affected by the absence of international standards for veterinary cancer registries (Brønden *et al*., 2007). In addition, the lack of guidelines leads to enormous differences in data collection and consolidation methods among existing veterinary cancer registries (Brønden *et al*., 2007; Vascellari *et al*., 2009). To achieve a more accurate comparison it is crucial to define international de jure standards for veterinary cancer registries. It is desirable to collect even more primary information from the canine tumour patient for further epidemiological studies of canine cancer, such as type of treatment, diet, age at neutering, obesity (body mass index) and body size, the presence of other diseases, vaccination status and environmental factors (e.g. exposure to cigarette smoke and other husbandry conditions, daily exercise).

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Conflict of Interest Statement

The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jcpa.2016.05.011.

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